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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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[REDACTED] EXAMINER

WILSON, MICHAEL C

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13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/750,240	HAMMOND ET AL.
	Examiner	Art Unit
	Michael C. Wilson	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 06 December 2002.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-101 is/are pending in the application.

4a) Of the above claim(s) 1-72,79-88,91-96 and 101 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 73-78,89,90 and 97-100 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ .
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>7 and 10</u> .	6) <input type="checkbox"/> Other: _____

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group VIII, claims 73-78, 89, 90 and 97-100, in Paper No. 12 is acknowledged. The traversal is on the ground(s) that it would not be undue burden to search claims of Group XIII in conjunction with the other claims. This is not found persuasive because the search is separate and the Groups require different considerations under enablement. The search and examination of all the groups together would be undue.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-72, 79-88, 21-96 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12.

Claim 101 has been added. Newly submitted claim 101 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: SEQ ID NO:10 is not a human AC_{VI} protein as claimed. Applicants point to support for claim 101 on pg 38, lines 20-30, which discusses non-human and non- AC_{VI} proteins. Therefore, the nucleic acid of claim 101 is patentably distinct from the nucleic acid encoding human AC_{VI} as claimed because it has a different structure and function. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 101 has been withdrawn

from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 73-78, 89, 90 and 97-100 are under consideration in the instant office action.

Claim Objections

Claims 73-78, 89, 90 and 97-100 are objected to because of the following informalities:

The phrase "a sequence encoding " in claim 73 should be --a nucleic acid sequence encoding--.

There should be a comma after "thereof" in claim 73.

The phrase "a sequence encoding " in claim 74 should be --a nucleic acid sequence encoding--.

The term "shown" in claim 75 should be --of--.

The term "An" in claims 76-78 should be --The--.

The term "a" in claim 89 and 90 should be --the--.

Claims 97-100 should begin with --The--, not "A".

Claim 97 and 99 should have a comma after "viral vector" to be in correct Markush format.

Claim 98 and 100 should have a comma after "adenoviral vector" to be in correct Markush format.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 73-78, 89, 90 and 97-100 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 73, 78, 89, 97 and 98 require a nucleic acid sequence encoding a human AC_{VI} protein or a variant thereof having adenylylcyclase activity. Claims 73, 89, 97 and 98 have function but no structure. Claim 78 requires a nucleic acid that "hybridizes at high stringency to a polynucleotide having the nucleotide sequence shown in SEQ ID NO:1 or 3 or 5. An adequate written description of a DNA requires more than a mere statement that it encodes human AC_{VI} or a variant thereof and has adenylylcyclase activity as in claims 73, 89, 97 and 98; what is required is a description of the structure of the DNA itself. It is also not sufficient to define AC_{VI} as being a "human" AC_{VI} protein, or variant thereof having adenylylcyclase activity (claims 73, 78, 89, 97 and 98) because it is unclear whether the protein must function in humans or must be isolated from humans and because activity is not specific to AC_{VI}. The structure of all DNA encoding proteins that have adenylylcyclase activity as broadly claimed in humans cannot be

envisioned. The structure of all DNA isolated from humans that have adenylylcyclase activity as broadly claimed cannot be envisioned. The structure in claim 78 is not specific to an AC_{VI} activity, a protein that functions in humans or a protein isolated from humans. In fact, the activity that is specific to AC_{VI} is not taught in the specification and cannot be envisioned. Naming a protein generically known to exist with the limitation of "human" and having a function that is not specific to AC_{VI}, in the absence of knowledge as to the structure of all AC_{VI} proteins that function in humans or are isolated from humans, is not a description of that genus. Thus, claiming all DNA's encoding proteins or variants thereof having a generic activity without defining the structure of the DNA or specifying the activity of the protein is not in compliance with the description requirement. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

Claims 74, 90, 99 and 100 require a nucleic acid sequence encoding a human AC_{VI} protein of SEQ ID NO:11. Use of the word "a" in "a human adenylylcyclase VI" is interpreted as encompassing allelic variants, fragments and homologs of SEQ ID NO:11. The claims do not require the protein of SEQ ID NO:11 has an activity. The specification does not teach any allelic variants, fragments and homologs of SEQ ID NO:11. Naming a protein generically known to exist in the absence of knowledge as to the structure of allelic variants, fragments or homologs of SEQ ID NO:11, is not a description of that protein. In particular, naming a fragment of SEQ ID NO:11 without a function that is specific to SEQ ID NO:11 is not adequate written description of such a protein. Thus, claiming all DNA's that encode allelic variants, fragments or homologs of

SEQ ID NO:11 without defining the structure of such DNA or claiming a function that is specific to SEQ ID NO:11, is not in compliance with the description requirement.

Replacing "a" with --the-- would overcome this rejection.

Claims 75-77 require a nucleic acid sequence encoding "a sequence of at least 100 nucleotides that has at least 95% overall sequence identity with" SEQ ID NO:1, 3, or 5. SEQ ID NO:5 is full length human AC_{VI}. SEQ ID NO:1 and 3 are fragments of SEQ ID NO:5. The claims do not require the DNA encodes a protein having any function, particularly one that is specific to AC_{VI}. It is noted that the claims are not limited to DNA that is at least 100 nucleotides in length having 95% identity with SEQ ID NO:1, 3 or 5 (see 112/2nd below). The specification teaches AC_{VI} has adenylylcyclase activity, which is generic to any AC protein, but does not teach an adenylylcyclase activity that is specific to AC_{VI}. An adequate written description of DNA generically known to exist requires more than stating it is at least 100 nucleotides in length and has at least 95% identity with SEQ ID NO:1,3 or 5. What is required is a description of the function of the DNA that correlates with the structure. It is not sufficient to define DNA solely by its structure because disclosure of no more than that, as in the instant case, is simply a wish to know other DNA sequences with that structure claimed having the function of SEQ ID NO:1, 3 or 5. Naming all DNA having the structure claimed in the absence of correlating the function is not a description of that DNA. Thus, claiming all DNA's that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived.

Claims 73-78, 89, 90 and 97-100 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 73, 78, 89, 97 and 98 require a nucleic acid sequence encoding a human AC_{VI} protein or a variant thereof having adenylylcyclase activity. Claims 73, 89, 97 and 98 have function but no structure. Claim 78 requires a nucleic acid that "hybridizes at high stringency to a polynucleotide having the nucleotide sequence shown in SEQ ID NO:1 or 3 or 5.

Claims 74, 90, 99 and 100 require a nucleic acid sequence encoding a human AC_{VI} protein of SEQ ID NO:11. Use of the word "a" in "a human adenylylcyclase VI" is interpreted as encompassing allelic variants, fragments and homologs of SEQ ID NO:11. The claims do not require the protein of SEQ ID NO:11 has an activity. The specification does not teach any allelic variants, fragments and homologs of SEQ ID NO:11.

Claims 75-77 require a nucleic acid sequence encoding "a sequence of at least 100 nucleotides that has at least 95% overall sequence identity with" SEQ ID NO:1, 3, or 5. SEQ ID NO:5 is full length human AC_{VI}. SEQ ID NO:1 and 3 are fragments of SEQ ID NO:5. The claims do not require the DNA encodes a protein having any function, particularly one that is specific to AC_{VI}. It is noted that the claims are not limited to DNA that is at least 100 nucleotides in length having 95% identity with SEQ ID

NO:1, 3 or 5 (see 112/2nd below). The specification teaches AC_{VI} has adenylylcyclase activity, which is generic to any AC protein, but does not teach an adenylylcyclase activity that is specific to AC_{VI}.

The only disclosed purpose for the DNA claimed is to encode functional protein.

The specification and the art at the time of filing did not teach one of skill in the art how to predict the structure of DNA having an activity that is specific to AC_{VI}, particularly human AC_{VI}. The specification does not provide adequate guidance for one of skill in the art to predict a function of AC_{VI} that is specific to AC_{VI}. The specification does not teach one of skill how to distinguish functional and non-functional proteins, how to distinguish AC_{VI} proteins from other proteins or human proteins from non-human proteins based on the structure of the DNA encoding such proteins. Thus, claiming DNA encoding a protein only by the structure as in claims 74-77 or only by function as in claim 73, 89, 97 and 98 in the absence of teaching one of skill in the art how to predict which DNA will have the desired function is not adequate guidance for one of skill to use the DNA as broadly claimed. In the case of claim 78, which has both structure and function, the function of the protein (claim 73) is generic to any AC protein ("adenylylcyclase activity") and is not specific to AC_{VI}. The specification and the art at the time of filing did not teach one of skill how to predict proteins having activity that is specific to AC_{VI}, particularly to human AC_{VI}, based on having generic the generic function of "adenylylcyclase activity." Therefore, it is unpredictable which of the DNA as broadly claimed in 78 encode proteins having a function that is specific to AC_{VI} or to humans. It would require one of skill in the art undue experimentation to determine

which DNA encode human proteins that have an adenylylcyclase activity that is specific to AC_{VI}.

In conclusion, the specification does not enable one of skill in the art at the time of filing to determine which DNA as broadly claimed encode human proteins that have an adenylylcyclase activity that is specific to AC_{VI}.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 73-78, 89, 90 and 97-100 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 73 is indefinite because it is unclear whether applicants consider canine or mouse AC_{VI} proteins variants of human AC_{VI} having adenylylcyclase activity as claimed. Non-human AC_{VI} proteins such as canine or mouse AC_{VI} proteins share significant homology with human AC_{VI} proteins and have adenylylcyclase activity as claimed. Therefore, it is unclear if the claim encompasses canine or mouse AC_{VI} proteins.

Claim 74 is unclear because SEQ ID NO:11 is only one protein, but the claim refers to "a human adenylylcyclase VI (AC_{VI}) polypeptide of SEQ ID NO:11," which implies there is more than one protein of SEQ ID NO:11. The claim should refer to –the human adenylylcyclase VI (AC_{VI}) polypeptide of SEQ ID NO:11—. If applicants are attempting to claim a nucleic acid sequence encoding a fragment of the protein in SEQ ID NO:11, such a limitation should be clearly set forth. In addition, the specification

does not teach how to distinguish a human protein of SEQ ID NO:11 from a non-human protein of SEQ ID NO:11. Nor does the specification teach how to distinguish an AC_{VI} protein from a non- AC_{VI} protein by providing an activity that is specific to AC_{VI}. Therefore, the metes and bounds of DNA encompassed by the claim cannot be determined.

Claim 75 is indefinite because “a sequence of at least 100 nucleotides that has at least 95% overall sequence activity with a nucleotide sequence of comparable length within the sequence shown SEQ ID NO:1 or 3 or 5” is unclear.

- a. “a sequence of at least 100 nucleotides” is unclear because it is unclear if the sequence is a portion taken from at least 100 nucleotides or if the sequence is 100 nucleotides in length.
- b. It is unclear whether the phrase “that has at least 95% overall identity” applies to the “sequence” or the “at least 100 nucleotides”.
- c. The limitation of “overall” sequence identity is unclear. It cannot be determined to what the term “overall” applies. Identity can be calculated a number of different ways. It cannot be determined whether “overall” further limits the type of “identity” or does not further limit the type of “identity”. Therefore, the metes and bounds of “overall sequence identity” cannot be determined.
- d. The metes and bounds of nucleotides sequences “of comparable length” cannot be determined. It cannot be determined whether the nucleotide sequence “of comparable length” must be same length as the “at least 100 nucleotides”. If the nucleic acid sequence “of comparable length” can be a different length, it

cannot be determined when the nucleotide sequence is no longer considered “comparable” in length.

e. The phrase “within the sequence shown SEQ ID NO:1 or 3 or 5” is unclear because it is missing a word after “shown.”

f. Reference to nucleic acid sequences should use the same terminology throughout the claim. Reference to a “sequence” or “the sequence of SEQ ID NO:1 or 3 or 5” and “a nucleotide sequence” is written is unclear as the scope may differ. For example, as written, “a sequence of at least 100 nucleotides” could mean an amino acid sequence derived from at least 100 nucleotides. The phrase “a nucleic acid sequence of at least 100 nucleotides that has at least 95% overall sequence activity with a nucleic acid sequence of comparable length within the nucleic acid sequence shown SEQ ID NO:1 or 3 or 5” would be clear (but would still be subject to the indefiniteness issues above in a-e).

The limitation of “overall” sequence identity is unclear in claim 76 for reasons cited above.

Claim 77 is unclear because the nucleotides sequences of SEQ ID NO: 1 is less than 1000 base pairs in length and cannot be greater than 1000 base pairs in length as claimed.

Claims 97 and 99 are indefinite because the metes and bounds of a “lipid-based vector” cannot be determined. The specification does not provide a definition of such

vectors and the art at the time of filing did not limit any vectors to being delivered using lipids.

Claims 98 and 100 are indefinite because it is unclear if "said vector" refers to the "viral vector" or the lipid based vector" recited in the parent claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 73-78, 89 and 90 are rejected under 35 U.S.C. 102(b) as being anticipated by Ishikawa (1993; GenBank AAQ4525) or Katsushika (1992, PNAS, Vol. 18, pg 8774-8778).

Ishikawa taught a nucleic acid sequence encoding canine AC_{VI}. The nucleic acid of Ishikawa is equivalent to Accession No. M94968 taught by Katsushika.

Canine AC_{VI} is equivalent to claim 73 because it shares significant homology with SEQ ID NO:1, 3 and 5, has adenylylcyclase activity, is a variant of human AC_{VI} and has adenylylcyclase activity in humans. Claim 74 is included because the DNA of Ishikawa encodes a fragment of SEQ ID NO:11 (see 112/2nd). The phrase "a sequence of" (claim 75) is being interpreted as --a portion of--. Therefore, claim 75 encompasses a

fragment of a nucleic acid sequence that is at least 100 nucleotides in length, wherein the fragment has 95% identity with a portion of SEQ ID NO:1, 3, or 5. The first 10 nucleotides of AAQ4525 are 100% identical to SEQ ID NO:1, 3 or 5 which is equivalent to claim 75. The first 149 nucleotides of AAQ4525 have greater than 99% identity with SEQ ID NO:1, 3 or 5 which is equivalent to claim 76. Claim 77 is included because SEQ ID NO:1 cannot have 1000 nucleotides as claimed (see 112/2nd rejection above) and because the first 1000 nucleotides of AAQ4525 have greater than 99% identity with SEQ ID NO:3 or 5. The sequence is a “vector” as in claims 89 and 90 because it is DNA isolated by genetic engineering and capable of being transfected into a host cell.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 73-78, 89 and 90 are rejected under 35 U.S.C. 102(e) as being anticipated by Tomlinson (US Patent 6,465,237, Oct. 15, 2002).

The nucleotide sequence of SEQ ID NO:1, 3 or 5 in the instant application only has priority back to WO 98/10085, filed Sept. 5, 1997. Applicants' claim to priority applications 60/048,933 (June 16, 1997) and 60/058,209 (Sept. 5, 1996) are not granted because the applications did not disclose SEQ ID NO:1, 3 or 5. Therefore, the

effective filing date of the claimed invention as it relates to SEQ ID NO:1, 3 or 5 is Sept. 5, 1997.

Tomlinson taught a nucleic acid sequence encoding human AC_{V1} (SEQ ID NO:1), which is 97% homologous to SEQ ID NO:1 in the instant application. The sequence of Tomlinson was disclosed in WO99/01547, filed July 1, 1998, and Application 08/886,550, filed July 1, 1997. Claim 74 is included because the DNA of Ishikawa encodes a fragment of SEQ ID NO:11 (see 112/2nd). Claim 76 is included because “a sequence of” is being interpreted as –a portion of--, i.e. a portion of the sequence taught by Tomlinson is greater than 99% identical to SEQ ID NO:1 in the instant application. Claim 77 is included because SEQ ID NO:1 cannot have 1000 nucleotides as claimed (see 112/2nd rejection above). The sequence is a “vector” as in claims 89 and 90 because it is DNA isolated by genetic engineering and capable of being transfected into a host cell.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 73-78, 89, 90 and 97-100 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Ishikawa (1993; GenBank AAQ4525) or Katsushika (1992, PNAS, Vol. 18, pg 8774-8778) in view of Iyengar (US Patent 6,034,071).

Ishikawa or Katsushika taught a nucleic acid sequence encoding canine AC_{VI} which is equivalent to claim 73-78 for reasons cited above in the 102 rejection. Ishikawa did not teach the nucleic acid was in an adenoviral vector. However, Iyengar taught putting a mammalian adenylylcyclase into an adenoviral vector. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention to put the DNA of Ishikawa or Katsushika into the adenoviral vector of Iyengar. One of ordinary skill in the art would have been motivated to put the nucleic acid of Ishikawa or Katsushika into the adenoviral vector Iyengar to express the AC_{VI} protein in cells *in vitro* as taught by Iyengar.

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Claims 73-78, 89, 90 and 97-100 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Tomlinson (US Patent 6,465,237, Oct. 15, 2002) in view of Iyengar (US Patent 6,034,071).

Tomlinson taught a nucleic acid sequence encoding SEQ ID NO:1 (human AC_{VI}), which is equivalent to claim 73-78 for reasons cited above in the 102 rejection. Tomlinson did not teach the nucleic acid was in an adenoviral vector. However, Iyengar taught putting a mammalian adenylylcyclase into an adenoviral vector. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention to put the DNA of Tomlinson into the adenoviral vector of Iyengar. One of ordinary skill in the art

would have been motivated to put the nucleic acid of Tomlinson into the adenoviral vector Iyengar to express the human AC_{VI} protein in cells *in vitro* as taught by Iyengar.

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-0120.

Questions of formal matters can be directed to the patent analyst, Dianiece Jacobs, who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-3388.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 308-4242.

Michael C. Wilson



MICHAEL WILSON
PRIMARY EXAMINER